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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,745	07/03/2001	Ronald W. Davis	STAN-153	3662

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EXAMINER
STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
1637	5

DATE MAILED: 07/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,745	DAVIS ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The hyperlinks are present in paragraphs [0015], [0016], [0064], [0090].

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a bioactive compound by detecting a stress response gene in yeast, does not reasonably provide enablement for identifying a bioactive compound by detecting a stress response gene in any other eucaryotic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants describe in detail procedures for identification of bioactive compounds by detecting an expression of a stress response gene (either in a wild type cell or in a cell comprising a stress response gene construct), but do not describe the procedure or provide scientific reasoning that this method would work in all of eucaryotic cells. The mammalian cells have different metabolic pathways than yeast, and the stress response mechanism in mammalian cells may differ from the one elicited in yeast cells (see Gotthardt et al., Int. J. Cancer, vol. 66, pp. 790-795, 1996).

Due to the large quantity of experimentation necessary to identify the effects of bioactive compounds on stress response in all of eucaryotic cell types, the lack of direction/guidance presented in the specification regarding identification of the effects of bioactive compounds on stress response in all of eucaryotic cell types, the absence of working examples directed to identification of the effects of bioactive compounds on stress response in all of eucaryotic cell types, the unpredictability of the effects of bioactive compounds in different organisms, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3, 5-7 and 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 3 is indefinite because of the limitation "... host cell is contains a heterozygous deletion...".

B) Claim 3 is indefinite because of the limitation "... relatively low ... increase in expression of the stress response gene ...". It is unclear what levels of gene expression are considered as "relatively low".

C) Claim 5 is indefinite because of the limitation "... an increase in expression of the reporter gene construct...". it is unclear what levels of gene expression are considered as "increased".

D) Claim 6 is indefinite because of the limitation "... relatively lower level of expression of the reporter gene ...". It is unclear what levels of gene expression are considered as "relatively lower".

E) Claim 7 recites the limitation "each strain" in line 3. There is insufficient antecedent basis for this limitation in the claim.

F) Claim 11 is indefinite because of the limitation "... a low ... level of expression of the stress response gene...". It is unclear what level of gene expression is considered as "low".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, 4, 5 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Bianchi et al. (Applied and Environ. Microbiol., vol. 65, pp. 5023-5027, November 1999).

Bianchi et al. teach testing antibacterial agents using *E. coli* cells transfected with stress response gene reporter constructs, comprising *lacZ* reporter gene and promoters induced by cold shock (*cspA*), cytoplasmic stress (*ibp*) or protein misfolding (*P3rpoH*). The antibacterial agents tested were carbenicillin, nalixidic acid, chloramphenicol, polymyxin, tetracycline, streptomycin and neomycin. β-galactosidase activity was monitored with time after addition of the drugs to cell culture. (Abstract; Figure 1; page 5024).

7. Claims 1, 2, 4, 5, 8, 9 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (J. Bacteriol., vol. 173, pp. 7429-7435, 1991).

Adams et al. teach detecting expression of heat shock genes (HSP82, HSP26, SSA1, SSA2, SSA4, HSC 82) in response to bioactive substances such as 1,10-phenantroline and thiolutin. The expression levels of HSP82 were induced three- to four-fold in the presence of 1,10-phenantroline and 5- to 10-fold in the presence of thiolutin (Abstract; page 7249, last two paragraphs; p. 7430; page 7431, paragraphs 4-6; Fig. 2 and 3).

In addition, a reporter gene construct, consisting of the promoter and 5' end of the HSP82 gene fused to E. coli lacZ gene was used to assess heat shock gene expression in response to the drugs (page 7431, the last paragraph; page 7432, paragraphs 1 and 2; Fig. 4).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Applied and Environ. Microbiol., vol. 65, pp. 5023-5027, November 1999).

Bianchi et al. teaches detection of antibiotic effects on bacterial cells by detection of stress response, but does not teach using bacteria derived from biological samples. Bianchi et al. teach that this method is a valuable tool for identifying and characterizing new antibacterial agents.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the method of Bianchi et al. to detect sensitivity of bacteria from a biological

sample to a drug. The motivation to do so, expressly provided by Bianchi et al., would have been that the method could be used over a wide range of antibiotic concentrations.

10. No references were found teaching or suggesting claims 3, 6, 7, 10-16, but they are rejected for other reasons.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TS
July 17, 2002 TS

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
7/17/02